PREPARING FOR PREP: FROM THEORY TO PRACTICE KEY POPULATIONS

Dr Oscar Radebe

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HE4LTH MEN top to bottom

SOUTH AFRICANS AND AMERICANS IN PARTNERSHIP TO FIGHT HIV/AIDS
PEPFAR

UNITED STATES AGENCY INTERNATIONAL DEVELOPMENT
USAID
FROM THE AMERICAN PEOPLE

PrePARING FOR THE END OF HIV

- Until recently there has been exciting new advances in clinical research focusing on HIV prevention for high risk groups .

- *New data on Prep studies have given researchers , scientist, politicians, clinicians to to respond to the continent's HIV epidemic on a global scale.*

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PrePARING FOR THE END OF HIV

THEORY
Scientific Research

IMPLEMENTATION PROCESS

PRACTICE
Prescribing Prep

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Why do We Need PrEP ?

- 7400 new infections daily
- (600 in SA women daily)
- 15 Million in MLIC need ART
- 5.2 Million on ART by 2010
- For every 1 on ART another 2 infected.

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Key Populations

Key populations are those most likely to be **exposed** to HIV or to **transmit** it.

- People who inject drugs
- Men who have sex with men (MSM)
- Commercial sex workers
- Transgender persons
- Prisoners
- Migrants

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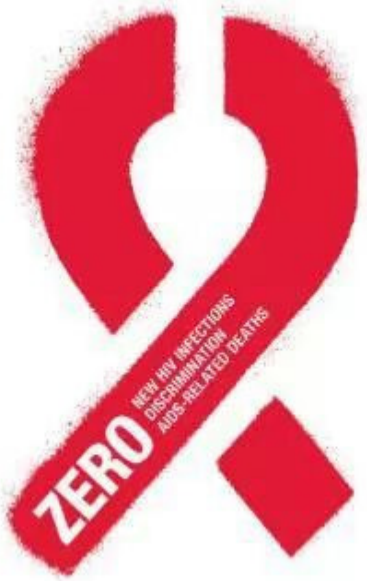
At Risk Populations in South Africa

- Young women15 to 24 years old
- Young people not attending school; girls who drop out of school
- People from low socio-economic groups
- People living close to national roads and in informal settlements
- Uncircumcised men
- Persons with disabilities and mental disorders
- Sex workers and their clients
- People who abuse alcohol and illegal substances
- Men who have sex with men
- Transgender persons



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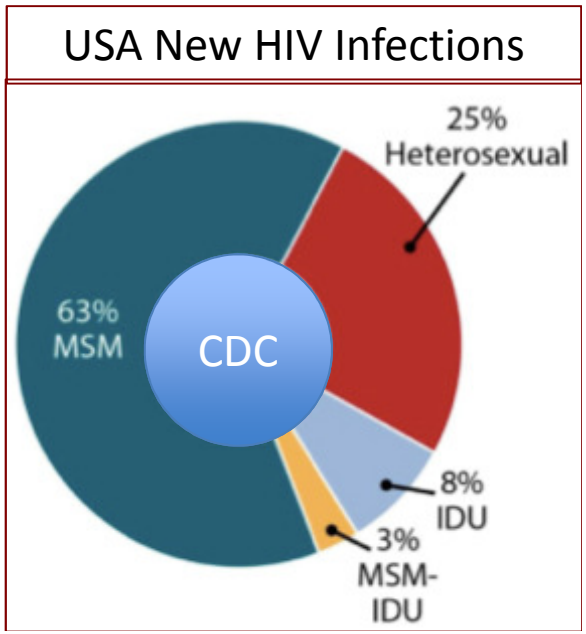
Why Prioritise MSM in a Predominantly Heterosexual Epidemic?

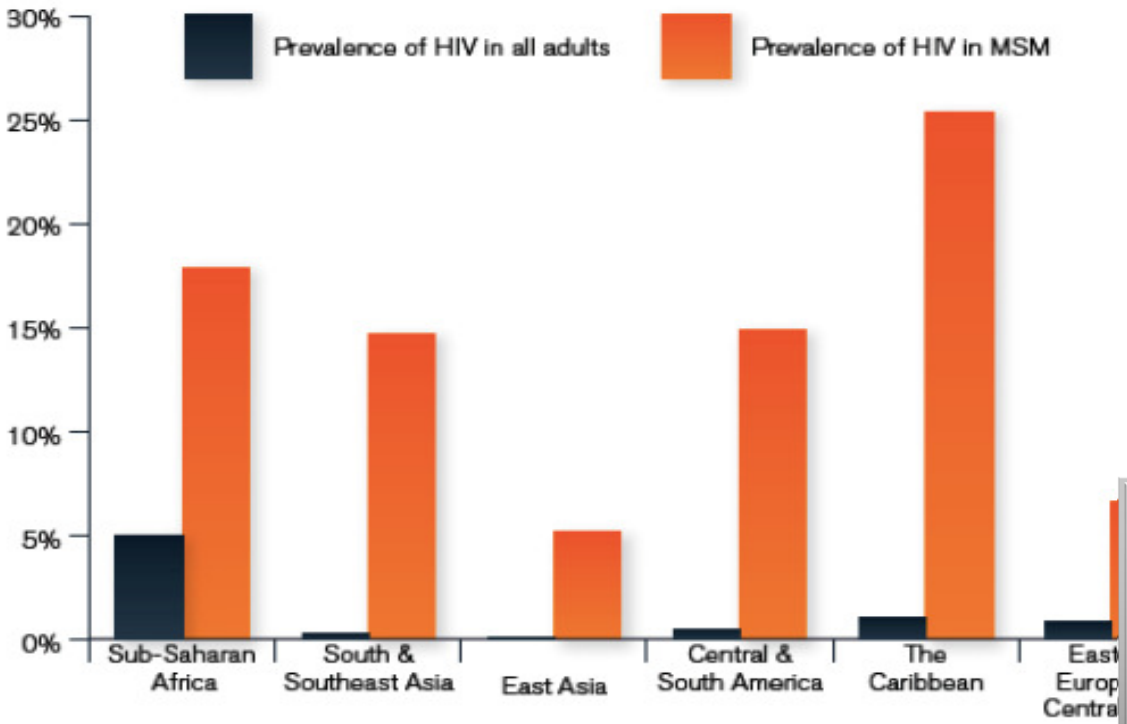
MSM are at high risk of HIV transmission and acquisition

- Gay and bisexual men account for **63% of new infections** in the US, and African American men in this group account for more new infections than any other subgroup.
- **Increased HIV risk** compared to general population (OR 3.8 in Africa) [Baral et al 2007]
- Soweto Men's Study MSM HIV prevalence = 20%
  - High rates of unprotected sex
  - High rates of sex with men and with women [Lane 2009]
- JEMS study, South Africa:
  MSM HIV prevalence = **43%** [HSRC 2009]



Global Prevalence of HIV in MSM

Gay men and other MSM shoulder a disproportionate burden of the HIV epidemic in virtually every country that reports reliable HIV surveillance data.



Prevalence of HIV in MSM compared with regional adult prevalence reported by UN 2010[1]

Beyrer C, Baral SD, van Griensven, et al, *Global epidemiology of HIV infection in men who have sex with men*, Lancet 2012.

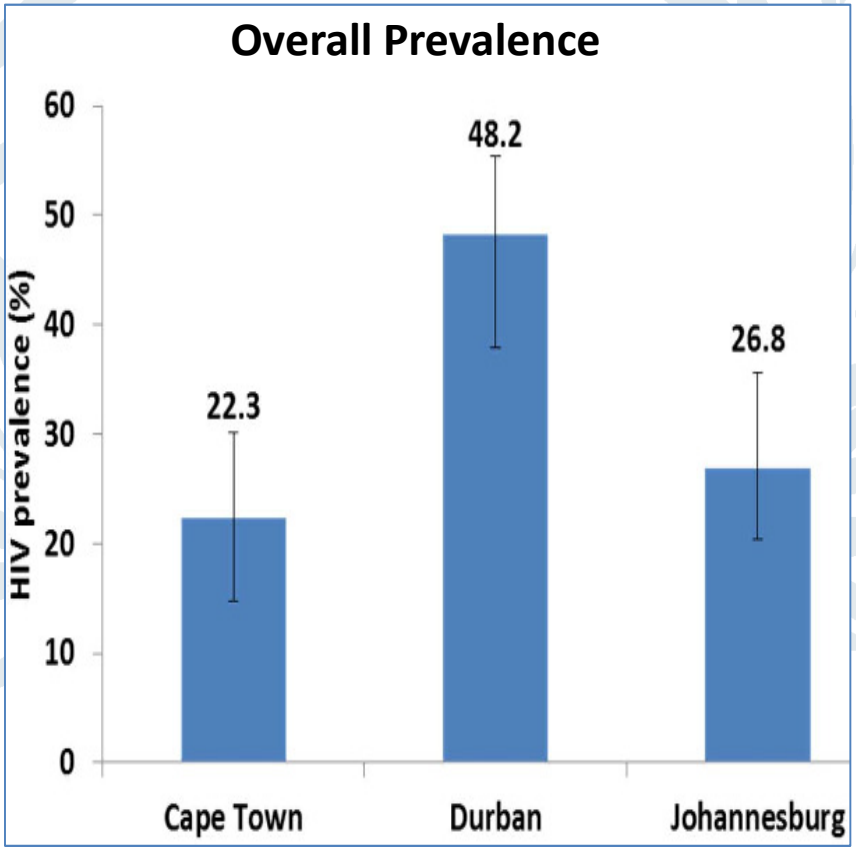
Key Population:

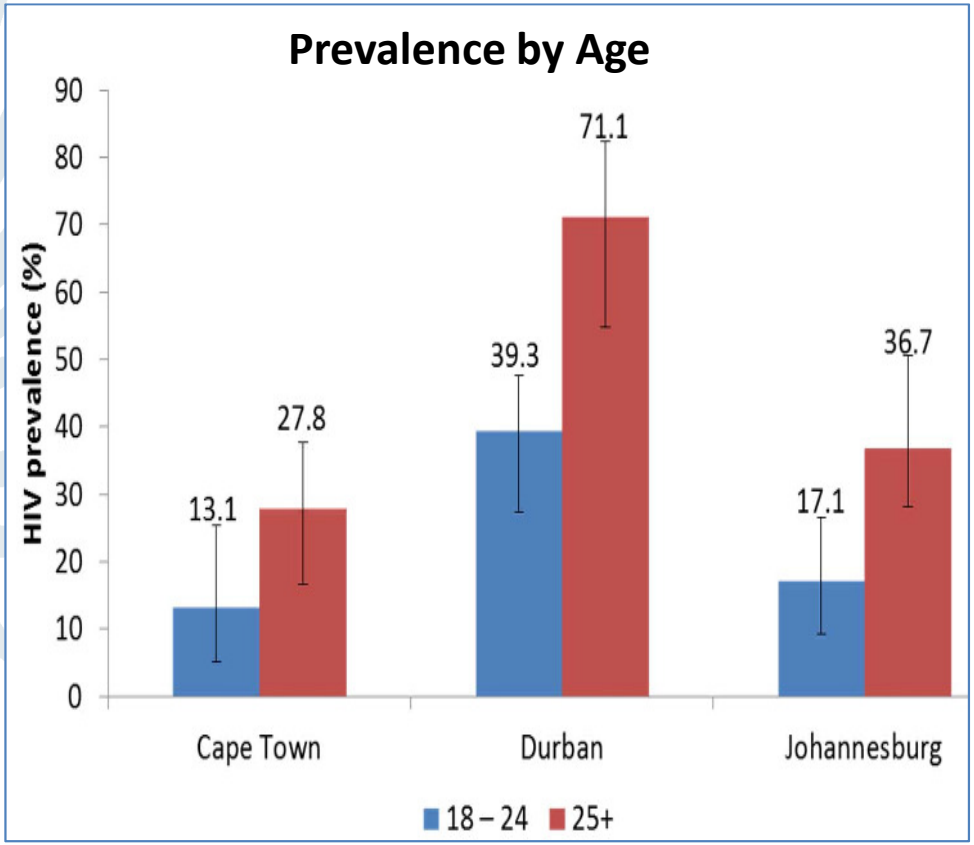
Relatively high HIV / STI Risk

AND

Relatively limited access to health services

HIV Prevalence





The South African Marang Men's Project

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Marang Study Summary

- Largest MSM Surveillance Study in SA
- Some methodological problems
  - Sex workers in Cape Town
  - Students in Durban
  - Jhb possibly the most representative
- High HIV rates and sub-optimal HIV knowledge
- High degrees of bisexuality and concurrency
- Ongoing risky behaviours (e.g. alcohol, low condom use and repeat HIV testing)
- Experience of stigma from health providers

The South African Marang Men's Project

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Risk of HIV Transmission

Type of contact	Transmission Risk (per 10,000)
Receptive anal intercourse	50
Receptive vaginal intercourse	10
Insertive anal intercourse	6.5
Insertive vaginal intercourse	5
Receptive oral intercourse	1
Insertive oral intercourse	0.5

UAI 20 times more risky than for vaginal

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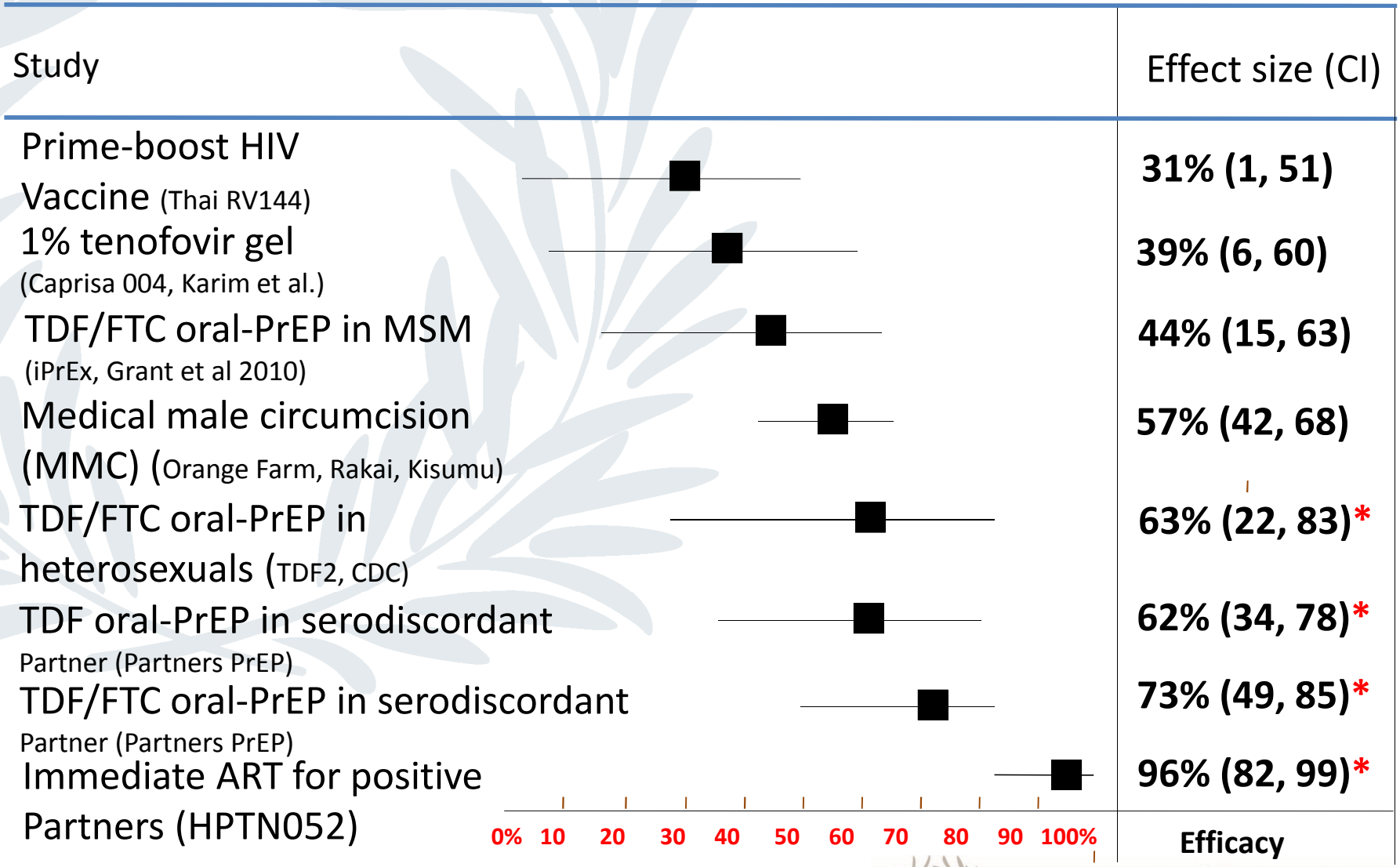
Novel HIV Prevention Intervention Efficacy



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ART-Based PrEP

How are antiretrovirals used?	• Oral pill
	• Topical gel (microbicide)
	  •Rectal
	  •Vaginal
	• Injection
	• Intravaginal ring

How often are the antiretrovirals used?	• Daily • Intermittently • Coitally (before/sex)
How many antiretrovirals are used?	• Combination • Monotherapy
What antiretrovirals are used?	• Truvada • Tenofovir •(Maraviroc)

Post Exposure prophylaxis (PEP)

Treatment as Prevention (TasP)

Combination Prevention with existing and new technologies

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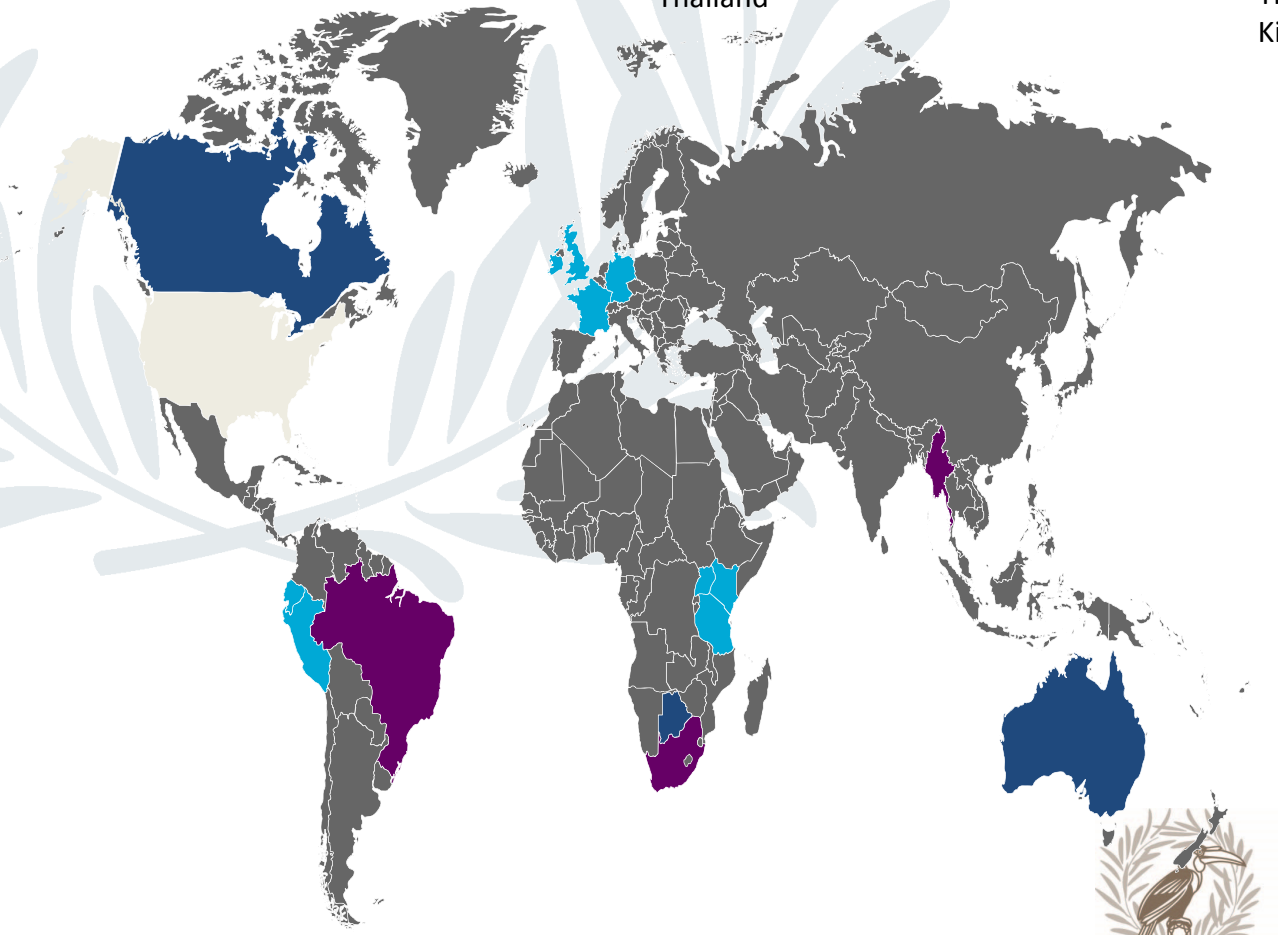
Regulatory Approval for Daily TDF/FTC for Prevention in Host Countries

TDF/FTC approved for prevention
United States

Regulatory application filed for a prevention indication for TDF/FTC
Brazil
South Africa
Thailand

Host countries with no regulatory application filed for prevention
Australia Botswana Canada
Ecuador France Germany
Kenya Peru Tanzania
Thailand Uganda United Kingdom



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Four Early Trials Demonstrating PrEP Efficacy in Diverse Geographic and Risk Populations

Study, population	PrEP agent	# of HIV infections		PrEP efficacy (95% CI) publication
		PrEP	placebo	
Partners PrEP Study Heterosexual couples Kenya, Uganda (n=4758)	TDF/FTC	13	52	**75%** (55-87%)
	TDF	17		**67%** (44-81%) Baeten et al. N Engl J Med 2012
TDF2 Study Heterosexuals Botswana (n=1219)	TDF/FTC	10	26	**62%** (16-83%) Thigpen et al. N Engl J Med 2012
Bangkok Tenofovir Study (BTS) IDUs Thailand (n=2413)	TDF	17	33	**49%** (10-72%) Choopanya et al. Lancet 2013
iPrEx MSM Brazil, Ecuador, Peru, South Africa, Thailand, US (n=2499)	TDF/FTC	36	64	**44%** (15-63%) Grant et al. N Engl J Med 2010

iPrEx

- Using ART in negative patients on a long term basis to reduce infection risk if they are exposed to the virus
- Seems safe
- High adherence
- Global iPrEx Study

2499 MSM &TG: Truvada daily pill vs placebo → 44 % reduction in HIV transmission (95% confidence interval, 15% to 63%: p = 0.005)

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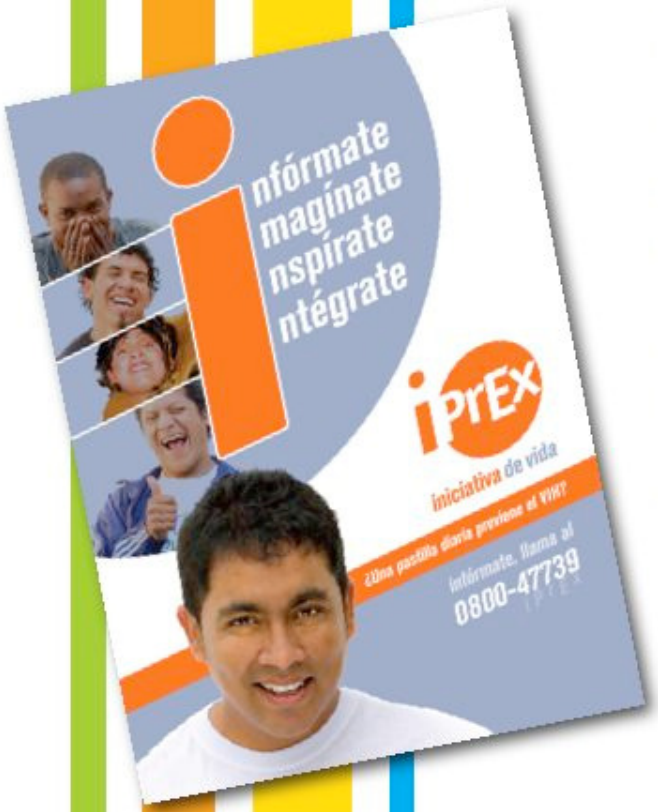
iPrEX Study Design & Results



- **High Risk MSM**
- **Randomized 1:1 Daily Oral PREP**
- **FTC/TDF vs Placebo**
- **Followed Monthly on Drug for:**
  - HIV seroconversion
  - Adverse Events
  - Metabolic Effects
  - HBV Flares among HBsAg+
  - Risk Behavior & STIs
  - Adherence
  - If Infected
    - *Drug Resistance*
    - *Viral Load*
    - *CD4+ T Cell Count*

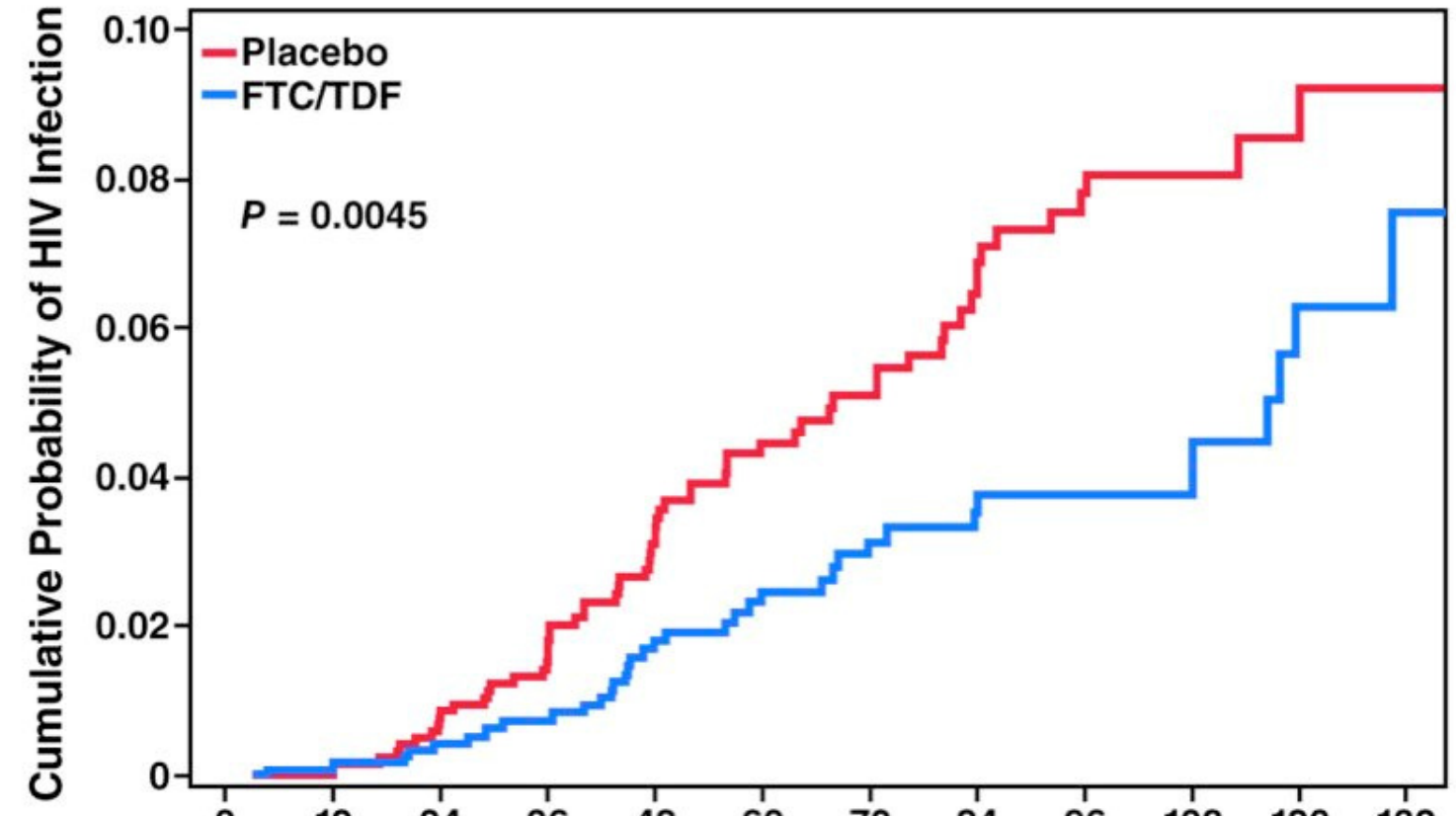
New England Journal of Medicine, online Nov 23, 2010

HIV Infections

110 in total (100 incident, 10 at baseline)

At least on specimen with undetectable RNA for all incident seroconverters

Efficacy (MITT) 44% (15-63%)
Infection Numbers: 64 – 36 = 28 averted

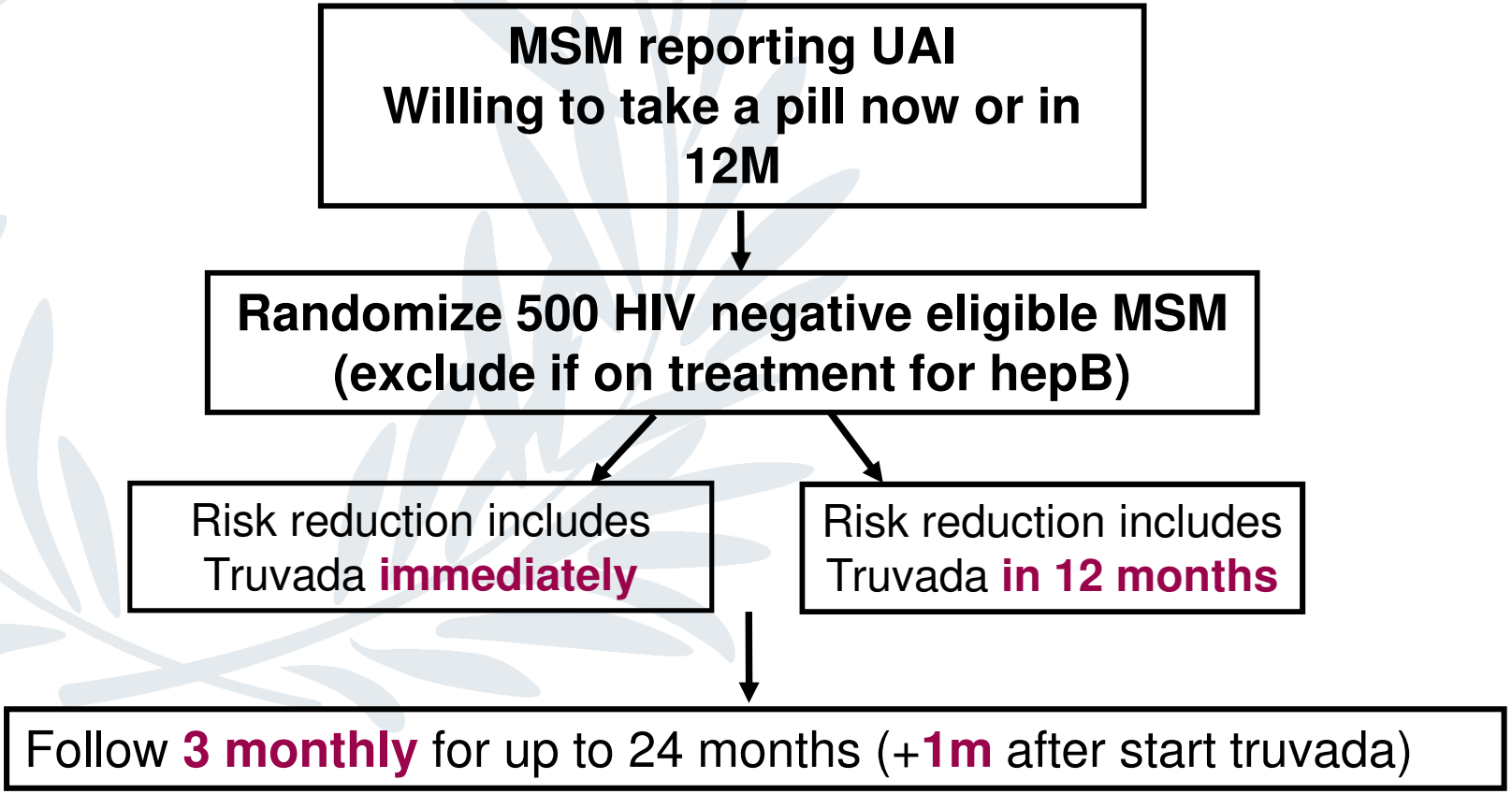


N =												
Placebo:	1248	1194	1108	1005	852	674	546	444	370	258	137	60
FTC/TDF:	1251	1188	1097	988	848	693	558	447	367	267	147	65

10.200B2

New England Journal of Medicine, online Nov 23, 2010

PROUD Study, United Kingdom



Outcome: HIV incidence in immediate vs deferred arm

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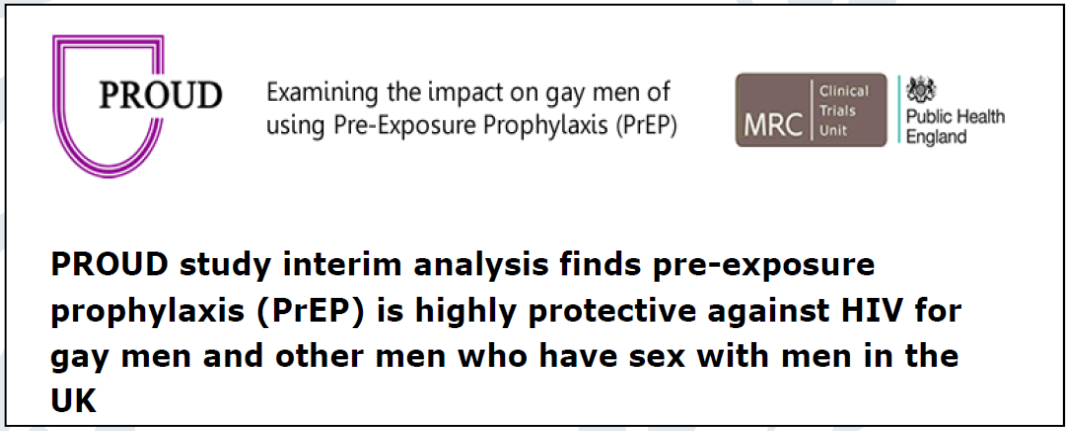
PROUD Study: Real World PrEP



Among MSM in the UK, delivery of PrEP (compared to randomization to deferred access to PrEP) *was so effective in preventing HIV* that the deferred arm was discontinued early.

– At baseline, the population was at considerable HIV risk: in the year prior to enrollment 25% had gonorrhea, 10% had syphilis, 40% used PEP, & 74% had recreational drug use

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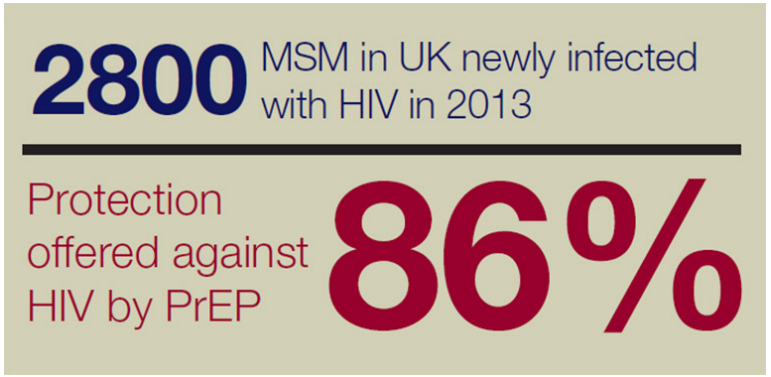
PROUD Study UK



- 545 MSM recruited to take Truvada PrEP
- Immediate or delayed initiation with 24 months follow up
- Study stopped early by DSMB as efficacy dictates that continuing would be unethical
- Efficacy =86% (90% CI: 58 – 96%) P-value =0.0002
- Number Needed to Treat =13 (90% CI: 9 – 25)
- HIV incidence amongst gay men in England is much higher than what was thought.
- There was no difference in the rate of STIs other than HIV
- The use of Truvada for PrEP was safe and concerns about resistance are minimal.
- PrEP can be delivered as part as routine HIV reduction package

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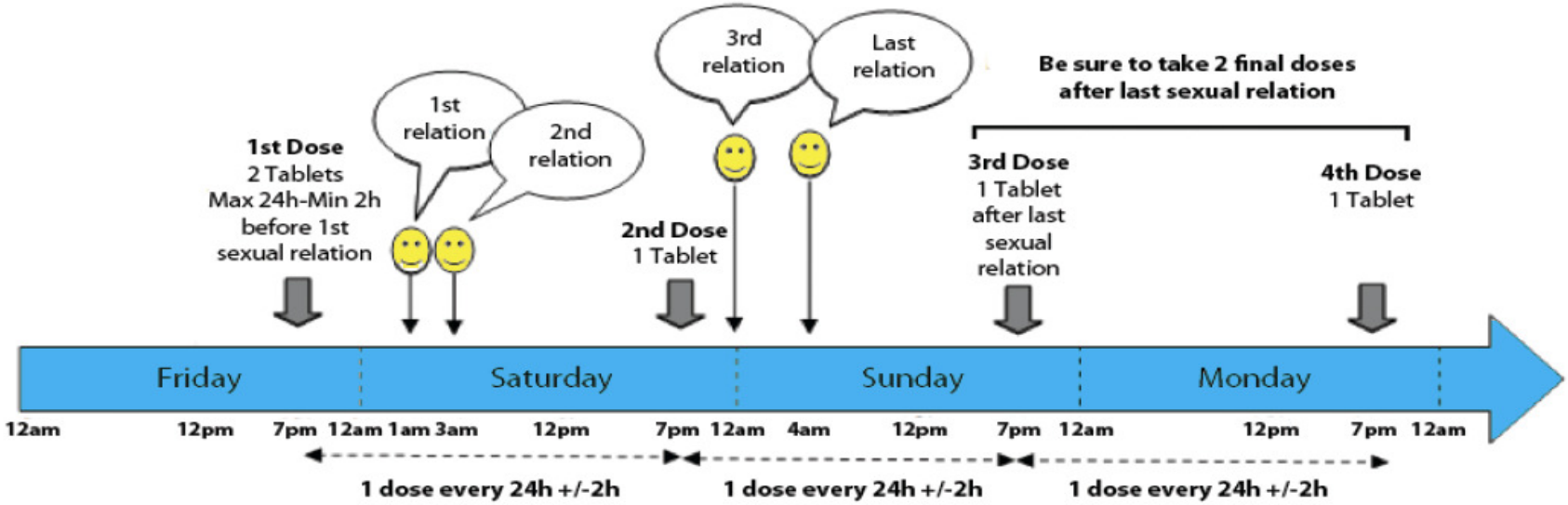
IPERGAY France



- RCT of Truvada versus placebo in 400 recruited high risk MSM
- Sex-based dosing (4 or more doses)
- Relative RR of HIV incidence was 86% (95% CI 40% to 99%, P = 0.002)
- Number needed to treat for 1 year to prevent 1 infection was 18.
- Also stopped early by DSMB because of high efficacy

86%

- Very sexually active
- Did they not by default get almost daily dosing?

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PrEP Works For High-risk People

Subgroup analyses of PrEP trials show that PrEP is effective for those at greatest HIV risk:

- Heterosexuals (Partners PrEP) Murnane et al. AIDS 2013
  - *Reporting sex without condoms*
  - *With an STI*
  - *With an HIV+ partner who has a high plasma HIV viral load*
  - *Women <30 years of age*
- MSM (iPrEx) Buchbinder et al. Lancet ID 2014; Solomon et al. Clin Infect Dis 2014
  - *Used cocaine*
  - *Had syphilis*
  - *Had anal sex with an HIV+ partner*
- HIV protection estimates for these subgroups were often higher than for the trial population as a whole, because adherence was often greater for persons taking greater risks

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PrEP Safety

- Rates of death, serious adverse events, and laboratory abnormalities (including renal dysfunction) were low and not significantly different between those taking PrEP and those taking placebo

- PrEP was well tolerated
  - Adverse effects occurred in minority of subjects
  - GI adverse effects (e.g., nausea) more common in those receiving PrEP than placebo
    - Occurred in < 10% and primarily during the first month only (PrEP "start up" symptoms)

- PrEP associated with a small change (~ 1%) in bone mineral density but no increased risk of fracture

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Adherence and HIV protection

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison	HIV protection estimate with high adherence
Partners PrEP TDF/FTC arm	81%	75%	90% (tenofovir in blood)
TDF2	79%	62%	78% (prescription refill)
BTS	67%	49%	70% - 84% (tenofovir in blood / pill count)
iPrEx	51%	44%	92% (tenofovir in blood)
FEM-PrEP & VOICE	<30%	No HIV protection	N/A

When adherence was high, HIV protection is consistent and high

Baeten et al N Engl J Med 2012; Thigpen et al N Engl J Med 2012; Choopanya et al Lancet 2013; Grant et al N Engl J Med 2010; Van Damme et al N Engl J Med 2012; Marrazzo et al CROI 2013

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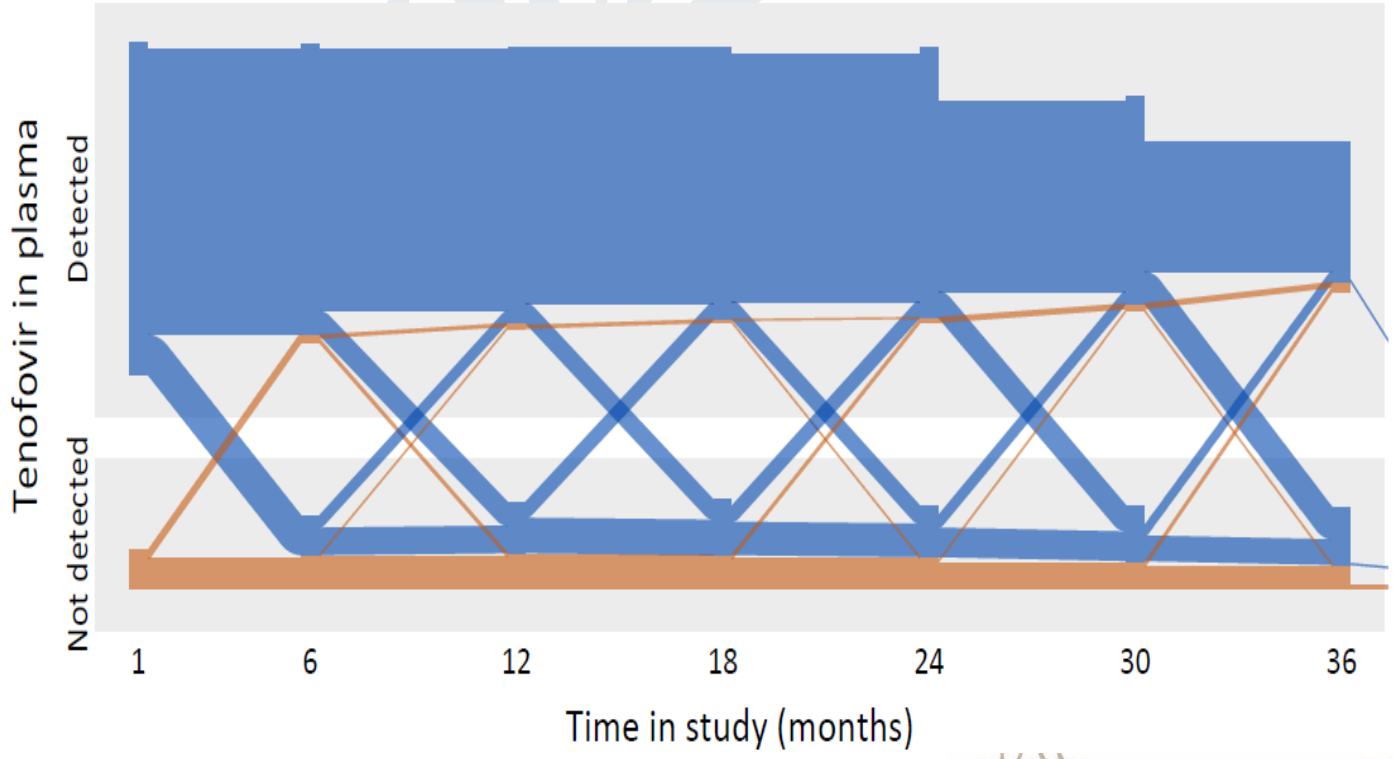
Oral PrEP Adherence

Longitudinal analysis of tenofovir detection in blood samples from persons on PrEP has show that, for those who were taking PrEP, adherence was frequently consistent over time:



Partners PrEP Study, Baeten et al., Lancet ID 2014

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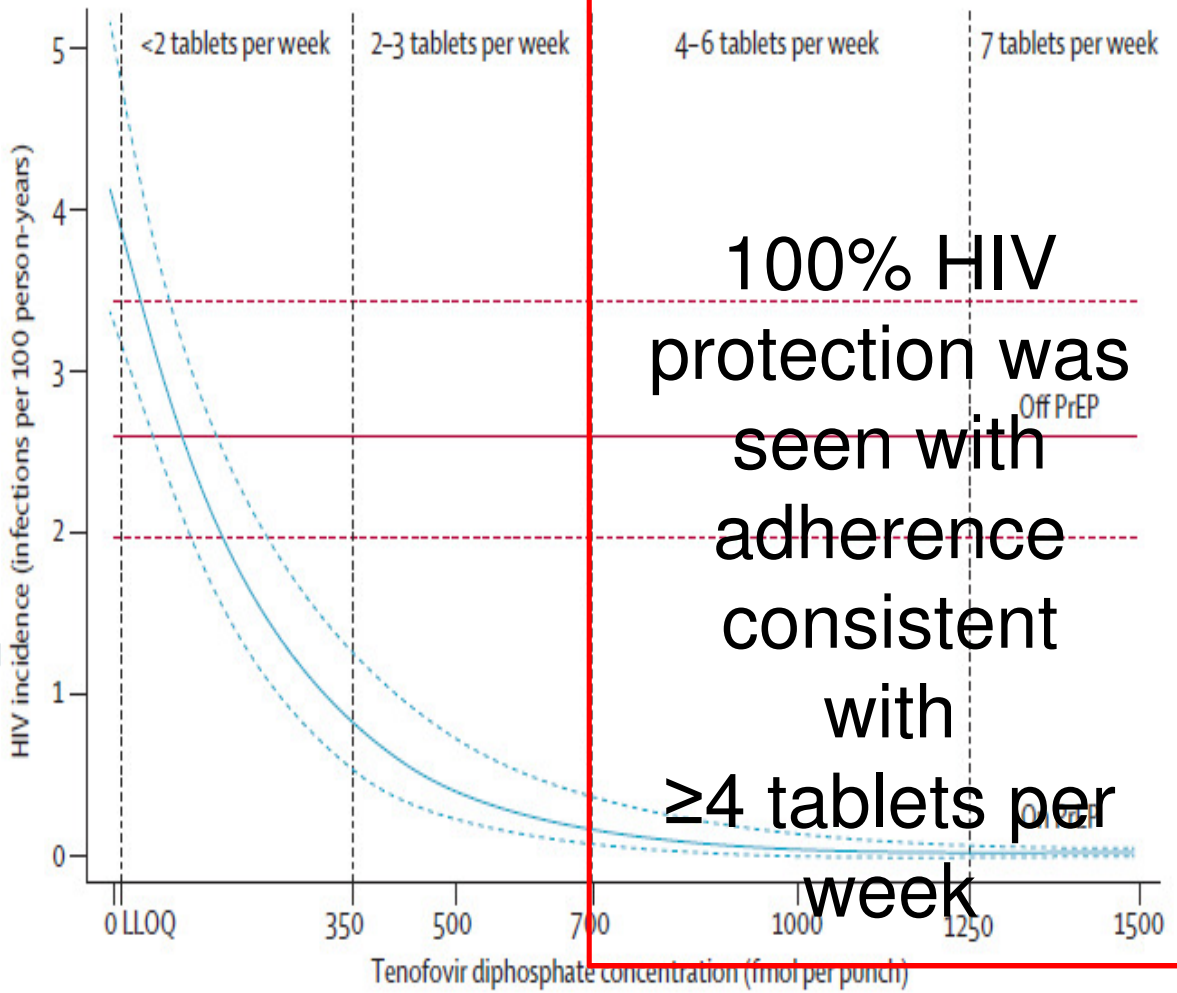
Perfect Adherence is Not Required: iPrEx OLE



100% HIV protection was seen with adherence consistent with ≥4 tablets per week

Grant et al. Lancet ID 2014

PrEP and ARV Resistance

Resistance from PrEP was very rare, with only a small number who had acute infection at the time they were started on PrEP.

	# of HIV seroconverters assigned PrEP with HIV resistance	
	HIV infected after enrollment	**Seronegative acute HIV infection at enrollment**
Partners PrEP	0 / 48	2 / 10
iPrEx	0 / 36	2 / 2
TDF2	0 / 10	1 / 1

Resistance = K65R (TDF) or M184V/I (FTC) mutations

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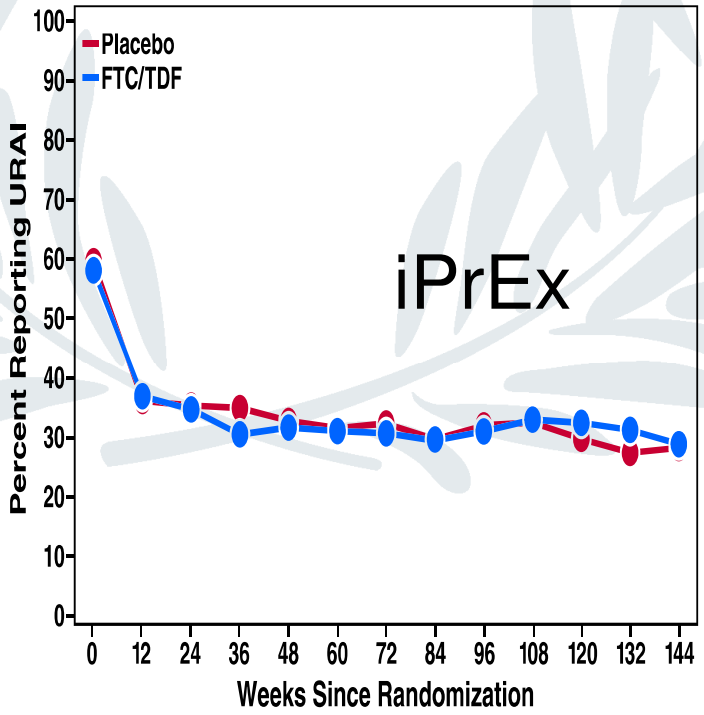
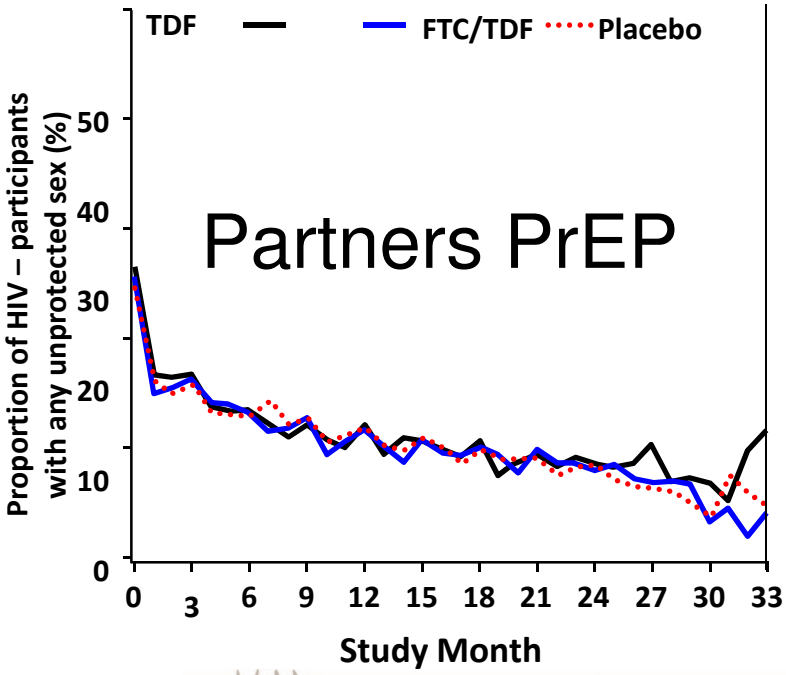
Risk compensation in PrEP clinical trials

In both iPrEx and Partners PrEP, unprotected sex and STIs were less common over time – suggesting synergy of ongoing risk-reduction counseling along with PrEP.





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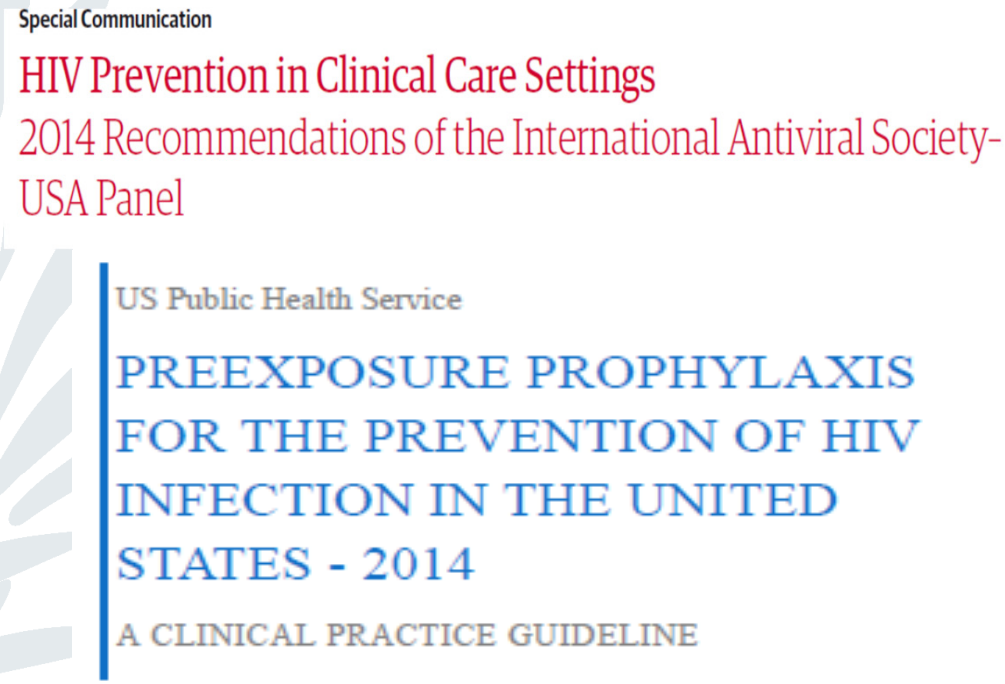
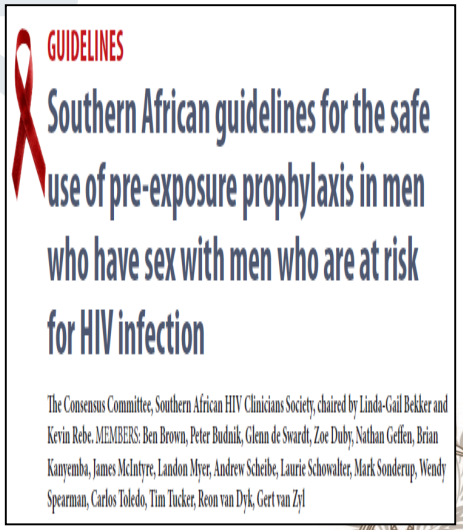
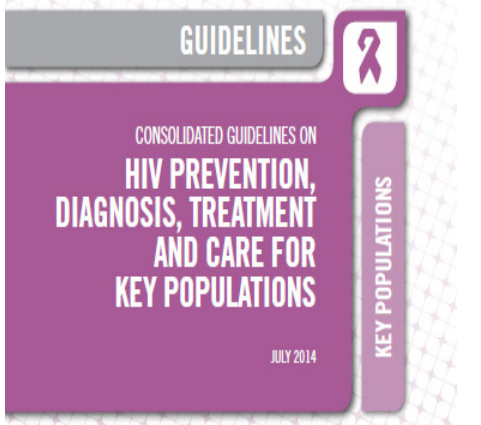
Prescribing PrEP

- **Risk assessment**
  - PrEP is indicated for those at high HIV risk
- **Eligibility**
  - HIV negative, adequate renal function, HBV testing
- **Follow-up**
  - Prescribe for daily use, periodic HIV testing (3-monthly), counsel about risk-reduction
- **PrEP Cycling**
  - PrEP is not meant to be life-long = for periods of highest risk







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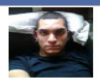
●●○○○ MTN-SA 8:46 AM 99%

PrEP Facts: Rethinking HIV Prevention a...



Does anybody know if there is a prep doctor in morgantown west virginia???

Like Comment

My six month PrEP anniversary tonight!

23 Likes 3 Comments

Like Comment

News Feed Requests Messenger Notifications More

●●○○○ MTN-SA 8:46 AM 99%

PrEP Facts: Rethinking HIV Prevention a...

):40 PM · Edited

Are you a **#PrEPWarrior**? Get the shirt to prove it. Team Friendly Northeast Ohio needs one more order in the next 6 hours for the fifth batch of these shirts to go into production!

#PrEPWarrior
Show your PrEP pride and help fight the stigma...
teespring.com

12 Likes 4 Comments

Like Comment Share

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Concerns About PrEP Delivery

- Who pays? (DOH keen but not committed)
- Bundling with other services (e.g., FP for women or HAST clinics, doctor or nurse driven)
- Community delivery to create demand and reduce burden on facilities?
- Minimise frequent visits and costs
- Risk screening for targeting (e.g. condomless anal receptive sex for MSM, risk score for serodiscordant couples)
- Adherence monitoring?

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Prep implementation process in South Africa

Preparation

Theory: Science &Research(Global and Local)

Implementing partners providing Technical assistance

Planning

NDOH buy in SANAC: LGBTI sector, all sectors/Political engagement

PROVINCIAL LEVEL

DISTRICT &SUB-DISTRICT LEVEL

FACILITY LEVEL

COMMUNITY – CREATE DEMAND

Practice

- Training & mentoring HCW on Prep
- Knowledge, acceptability of Prep as part of prevention of KP
- Constant supply of Prep
- Monitoring side effects of Prep

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USAID FROM THE AMERICAN PEOPLE

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Thank You

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